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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,808	02/19/2002	Manas Kumar Majumdar	08702.0086-00000	7146

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EXAMINER
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WOODWARD, CHERIE MICHELLE

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 11/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/078,808

Applicant(s)

MAJUMDAR ET AL.

Examiner

Cherie M. Woodward

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 18 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 21, 23-29 and 31-37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21, 23-29 and 31-37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Formal Matters*

1. Applicant's Reply and Amendments, filed 18 September 2006, are acknowledged. Claims 21, 23-29, and 31-37 are pending and under examination.

### *Response to Arguments*

#### *Claim Objections/Rejections Withdrawn*

2. The rejection of claims 21, 23-29, and 31-37 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,761,887 (Kavalkovich *et al*, PCT Pub WO 00/29552, (the '887 patent), is withdrawn in light of Applicant's Amendments, filed 18 September 2006. However, see the new rejection, necessitated by amendment, below.

3. The requirement for a priority showing under 37 CFR 41.202(d)(1) is withdrawn in light of Applicant's amendments to the claims.

### *New Claim Rejection – Necessitated by Amendment*

#### *Claim Rejections - 35 USC § 103*

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly

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owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 21, 23-29, and 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,761,887 (Kavalkovich *et al.*, PCT Pub WO 00/29552, (the '887 patent) in view of Minas *et al.*, (Orthopedics 1997 Jun; 20(6):525-38).

The claims recite a method for inducing chondrogenesis comprising administering to a patient an effective amount of a composition comprising autologous non-tissue culture expanded CD105+ cells isolated from the patient's bone marrow and a suitable matrix carrier; further comprising administering a protein selected from the TGF- $\beta$  superfamily of proteins, wherein the protein is capable of inducing the formation of cartilage tissue; wherein said protein is a BMP; wherein the BMP is BMP-2 or BMP-9; a method for treating arthritis comprising administering to a patient an effective amount of a composition comprising autologous non-tissue culture expanded CD105+ cells isolated from the patient's bone marrow and a suitable matrix carrier; a method for treating articular cartilage defects or damage comprising administering to a patient an effective amount of a composition comprising autologous non-tissue culture expanded CD105+ cells isolated from the patient's bone marrow and a suitable matrix carrier; a method for repairing cartilage tissue comprising administering to a patient an effective amount of a composition comprising autologous non-tissue culture expanded CD105+ cells isolated from the patient's bone marrow, a suitable matrix carrier, and a protein selected from the TGF- $\beta$  superfamily of proteins, wherein the protein is capable of inducing the formation of cartilage tissue; wherein said protein is BMP; wherein said proteins is BMP-2 or BMP-9; further comprising administering protein selected from the TGF- $\beta$  superfamily of proteins, wherein the protein is capable of inducing the formation of cartilage tissue; wherein said protein is a BMP, wherein the BMP is BMP-2 or BMP-9.

Kavalkovich *et al.*, teach a method for inducing chondrogenesis using an alginate layer system formed by seeding mesenchymal stem cells (MSCS) in alginate. These MSCS are known in the art to express CD105 (endoglin) (see, for exemplary purposes only, Barry *et al.*, Biochem. Biophys. Res. Comm. 1999, vol. 26541), pp. 134-139; previously cited in the Office Actions of 26 September 2003). Kavalakovich *et al.*, teach that alginate constructs can be formed using non-cultured populations of MSCS (p. 10, lines 10-19) and that the constructs can be used for cartilage regeneration (p. 5, lines 26-28) and

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BMP-2 can be included as a chondrogenic agent (p. 8, lines 21-24). Kavalkovich et al., do not specifically teach a method for inducing chondrogenesis comprising administering autologous non-tissue culture expanded CD105+ cells.

Minas et al., teach the use of autologous cells in allografts and autologous chondrocyte implantation. Minas et al., teach the benefits of autologous cells, including eliminating the known side effects of non-autologous allografts of material that increase the risk of viral transmission, low chondrocyte viability, and the potential for an antigenic immune response against the transplanted cells. The use of autologous cells offers the opportunity to achieve biologic repair without the ensuing complex issues of non-autologous cell rejection or an antigenic or immune response against the non-autologous cells (see pp. 531-535).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to combine the teachings of the Kavalakovich with the teachings of Minas et al., to use autologous CD105+ cells with BMP-2 as a factor that would induce chondrogenesis because BMP-2, a well-known member of the TGF- $\beta$  superfamily, known to be involved in chondrogenesis and has been shown to interact with endoglin (CD 105) and use of autologous cells offers the opportunity to achieve biologic repair without the ensuing complex issues of non-autologous cell rejection or an antigenic or immune response against the non-autologous cells. The person of ordinary skill in the art would have been motivated to make those modifications because the use of autologous cells is extremely beneficial to the patient without the inherent side effects of non-autologous allografts of material that increase the risk of viral transmission, low chondrocyte viability, and the potential for an antigenic immune response against the transplanted cells.

#### *Conclusion*

**NO CLAIM IS ALLOWED.**

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action

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is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Thursday 9:00am-7:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CMW

AU 1647

*Marianne P. Allen*

MARIANNE P. ALLEN  
PRIMARY EXAMINER

*AU 1647*

*11/1/06*